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2002 Rec'd PTO 05 MAR 2002

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Commissioner of Patents and Trademarks,  
Washington, D.C. 20231 on February 15, 2002.

Patent Application  
Docket No. SPO-112  
Serial No. 09/762,842

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TECH CENTER 1600/2900

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Akira Murasugi, Yukio Asami, Isao Kido, Hideshi Kumai  
Serial No. : 09/762,842  
Conf. No. : 1096  
Filed : February 12, 2001  
For : High Level Secretary Expression System of Intact MK Family Protein

Office of Initial Patent Examination  
Customer Service Center  
Commissioner of Patents and Trademarks  
Washington, D.C. 20231

REQUEST FOR CORRECTION OF FILING RECEIPT

Sir:

The applicants respectfully request the correction of error in the official Filing Receipt for the above-identified patent application. A clerical error has occurred in the title of the application. The correction needed is as follows:

Title

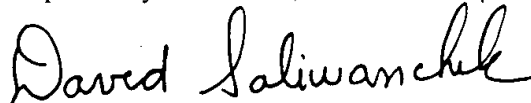
Mass secretion/expression system of true mk family protein

should read

**High Level Secretary Expression of Intact MK Family Protein**

A copy of the erroneous Official Filing Receipt accompanies this Request. Also, attached is a copy of page 1 of the Transmittal Letter Form PTO-1390 and page 1 of the subject specification. Correction of the above is respectfully requested.

Respectfully submitted,



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DRP/la

Enclosures: Copy of erroneous Filing Receipt;  
Page 1 of Form PTO-1390; and  
Page 1 of subject application.



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DESCRIPTION

HIGH LEVEL SECRETORY EXPRESSION SYSTEM OF INTACT MK FAMILY PROTEIN

5 Technical Field

The present invention relates to a high level secretory expression system of an intact MK family protein by recombinant DNA techniques using methylotrophic yeast as the host.

10 Background Art

MK is a growth factor discovered as the retinoic acid responsive gene product, and is a polypeptide that is rich in basic amino acids and cysteine and that has the molecular weight 13 kDa (Kadomatsu, K. et al.: Biochem. Biophys. Res. Commun., 151: 1312-1318, 1988; 15 Tomomura, M. et al.: J. Biol. Chem., 265: 10765-10770, 1990). MK has 45% sequence homology to another heparin-binding protein referred to as pleiotrophin (PTN) or heparin-binding growth associated molecule (HB-GAM).

MK and PTN have common activities such as the neurotrophic factor activity (Li, Y.-S. et al.: Science, 250: 1690-1694, 1990; Merenmies, 20 J. & Rauvala, H.: J. Biol. Chem., 265: 16721-16924, 1990; Muramatsu, H. et al.: Dev. Biol., 110: 284-296, 1985), the enhancement of fibrinolytic system (Kojima, S. et al.: J. Biol. Chem., 270: 9590-9596, 1995), proliferation of various cells, transformation of NIH3T3 cells 25 (Kadomatsu, K. et al.: Brit. J. Cancer, 75: 354-359, 1997; Yokota, C. et al.: J. Biochem., 123: 339-346, 1998), and angiogenesis.

Thus, these MK family proteins are expected to be useful as drugs, and the development of high level expression system of these proteins has been strongly demanded. Natural MK and PTN proteins are 30 not glycosylated. Therefore, the high level expression of these proteins with no glycosylation by recombinant DNA techniques, would be extremely useful not only for production of the proteins as drugs but also for structural and functional analyses of the proteins. In this invention, an unglycosylated MK family protein is referred to 35 as an intact MK family protein. Herein, an MK family protein means a protein comprising at least the amino acid sequence of a mature



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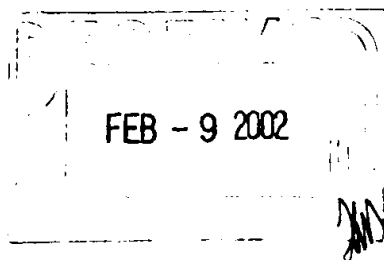
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WASHINGTON, D.C. 20231  
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APPLICATION NUMBER	FILING DATE	GRP ART UNIT	FIL FEE REC'D	ATTY. DOCKET NO.	DRAWINGS	TOT CLAIMS	IND CLAIMS
09/762,842	04/30/2001	1646	1120	SPO-112	17	14	1

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CONFIRMATION NO. 1096

FILING RECEIPT



\*OC000000007334137\*

Date Mailed: 01/28/2002

Receipt is acknowledged of this nonprovisional Patent Application. It will be considered in its order and you will be notified as to the results of the examination. Be sure to provide the U.S. APPLICATION NUMBER, FILING DATE, NAME OF APPLICANT, and TITLE OF INVENTION when inquiring about this application. Fees transmitted by check or draft are subject to collection. Please verify the accuracy of the data presented on this receipt. If an error is noted on this Filing Receipt, please write to the Office of Initial Patent Examination's Customer Service Center. Please provide a copy of this Filing Receipt with the changes noted thereon. If you received a "Notice to File Missing Parts" for this application, please submit any corrections to this Filing Receipt with your reply to the Notice. When the USPTO processes the reply to the Notice, the USPTO will generate another Filing Receipt incorporating the requested corrections (if appropriate).

**Applicant(s)**

Akira Murasugi, Tokyo, JAPAN;  
Yukio Asami, Kanagawa, JAPAN;  
Isao Kido, Kanagawa, JAPAN;  
Hideshi Kumai, Kanagawa, JAPAN;

**Domestic Priority data as claimed by applicant**

THIS APPLICATION IS A 371 OF PCT/JP99/04332 08/10/1999

**Foreign Applications**

JAPAN 10/236621 08/10/1998  
JAPAN 11/84583 03/26/1999

**Projected Publication Date:** Not Applicable, filed prior to November 29,2000

**Non-Publication Request:** No

**Early Publication Request:** No

**Title**

High Level Secretory Expression System of Intact MK  
Family Protein

Mass secretion/expression system of true mk family protein

**Preliminary Class**

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FORM PTO-100  
REV. 9-10-00

DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE

ATTORNEY'S DOCKET NUMBER

TRANSMITTAL LETTER TO THE UNITED STATES  
DESIGNATED ELECTED OFFICE (DO/EO/US)  
CONCERNING A FILING UNDER 35 U.S.C. 371

SP0-112

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U.S. APPLICATION NO. (if known, see 37 CFR 1.51)

INTERNATIONAL APPLICATION NO.

PCT/JP99/04332

INTERNATIONAL FILING DATE

10 August 1999

PRIORITY DATE CLAIMED

26 March 1999  
10 August 1998TITLE OF INVENTION High Level Secretory Expression System Of Intact  
MK Family ProteinAPPLICANT(S) FOR DO/EO/US Akira Murasugi, Yukio Asami,  
Isao Kido, Hidesh Kumai

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. ☒ This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371.
2. ☐ This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. 371.
3. ☒ This is an express request to promptly begin national examination procedures (35 U.S.C. 371(f)).
4. ☒ The US has been elected by the expiration of 19 months from the priority date (PCT Article 31).
5. ☒ A copy of the International Application as filed (35 U.S.C. 371(c)(2)).
  - a. ☐ is attached hereto (required only if not communicated by the International Bureau).
  - b. ☒ has been communicated by the International Bureau.
  - c. ☐ is not required, as the application was filed in the United States Receiving Office (RO/US).
6. ☐ An English language translation of the International Application as filed (35 U.S.C. 371(c)(7)).
7. ☐ Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3)).
  - a. ☐ are attached hereto (required only if not communicated by the International Bureau).
  - b. ☐ have been communicated by the International Bureau.
  - c. ☐ have not been made; however, the time limit for making such amendments has NOT expired.
  - d. ☐ have not been made and will not be made.
8. ☐ An English language translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).
9. ☒ An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)). (unsigned)
10. ☐ An English language translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).

Items 11 to 16 below concern document(s) or information included:

11. ☐ An Information Disclosure Statement under 37 CFR 1.97 and 1.98.
12. ☐ An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
13. ☒ A **FIRST** preliminary amendment.  
☐ A **SECOND** or **SUBSEQUENT** preliminary amendment.
14. ☐ A substitute specification
15. ☐ A change of power of attorney and/or address letter
16. ☒ Other items or information. Submission of Sequence Listing Under 37 CFR 1.821-1.825